--29. An assay for a biologically derived denatured DNA or RNA test substance, which has a known normal nucleotide sequence and a known possible mutation at at least one target nucleotide position in said sequence, which assay determines whether the test substance has said normal nucleotide sequence or said possible mutation, said assay comprising the steps of

(a) annealing a target oligonucleotide probe of predetermined sequence to a first sequence of said test substance so that said target nucleotide position is aligned with a nucleotide in an end region of said target probe,

(b) annealing an adjacent oligonucleotide probe of predetermined sequence to a second sequence of said test substance contiguous to said first sequence, so that the terminal nucleotide in said end region of said target probe and one end of said adjacent probe are directly adjacent to each other,

(c) contacting said annealed target probe and adjacent probe with a linking agent under conditions such that the directly adjacent ends of said probes covalently bond to form a linked probe product unless there is nucleotide base pair mismatching between said target probe and said test substance at the target nucleotide position,

(d) separating said test substance and linked probe product, if formed, and

(e) detecting whether or not said linked probe product is formed as an indication of nucleotide base pair matching or mismatching at said target nucleotide position.

30. The assay of claim 1 in which said target probe or said adjacent probe is labeled and said detecting is performed by directly or indirectly detecting said label.

31. The assay of claim 2 in which said label is selected from the group consisting of a radioactive tag, an enzyme, a fluorescent tag, and a colorimetric tag.

32. The assay of claim 2 performed in a fluid medium in which only one of said target probe and said adjacent probe is labeled and the non-labeled one is immobilized, said method further comprising, prior to step (e), separating the immobilized linked probe product from the remainder of the fluid medium, and said detecting is performed by detecting the presence of said label contained by said immobilized linked probe product.

33. The assay of claim 4 wherein said target probe or said adjacent probe is immobilized by a covalent bond or by an affinity bond.

34. The assay of claim 2 wherein said test substance is immobilized.

35. The assay of claim 2 performed in a fluid medium in which only one of said target and said adjacent probes is labeled and in which both of said probes are in solution during steps (a), (b), and (c), said method further comprising immobilizing the non-labeled probe before step (e), and said detecting is performed by detecting the presence of said label on said immobilized linked probe product.

36. The assay of claim 1 together with the steps of (f) annealing a second adjacent oligonucleotide probe of predetermined sequence to a third sequence of said test substance contiguous with the end of said target or said adjacent probe opposite its facing end, and

(g) contacting said second adjacent probe with a linking agent to link it with said contiguous target or said adjacent probe.

37. The assay of claim 1 in which said linking agent is a ligase, and said linking occurs by ligation.

38. The assay of claim 2 together with the step of (f) placing the reaction mixture of step (d) in a migration medium in which said target and said adjacent probes, individually migrate at substantially different rates than said linked probe product, and in which said detecting occurs by detecting the position of labeled probe in said migration medium as a function of time.

39. The assay of claim 1 further comprising the step of:

(f) annealing to a second test substance a second oligonucleotide probe with substantially the same sequence as said target probe except that it contains a different nucleotide in at least one of said end nucleotide positions, said target and said second probes being labeled with different labels, wherein said detection step distinguishes between said labels.

40. The assay of claim 1 in which the normal nucleotide is present at said target nucleotide position.

41. The assay of claim 1 in which a mutant nucleotide is present at said target nucleotide position.

42. The assay of claim 1 in which said test substance is formed of DNA.

43. The assay of claim 1 in which said test substance is formed of RNA.

44. The assay of claim 1 wherein said end region of said target probe consists of the end nucleotide of said target probe and the three nucleotides adjacent to it.

45. The assay of claim 1 wherein said end region of said target probe consists of the end nucleotide of said target probe and the nucleotide adjacent to it.

46. The assay of claim 1 wherein said test substance comprises DNA sequences derived from genomic DNA.

47. The assay of claim 18 wherein said DNA sequences include sequences encoding all or part of normal β-globin or sickle β-globin gene.--

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